

# PATENT ABSTRACTS OF JAPAN

(11)Publication number : **08-217688**

(43)Date of publication of application : **27.08.1996**

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(51)Int.Cl.

A61K 35/78  
A61K 7/00  
A61K 7/48  
A61K 9/00

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(21)Application number : **07-067170**

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(22)Date of filing : **15.02.1995**

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## **(54) HYALURONIDASE INHIBITOR**

### **(57)Abstract:**

**PURPOSE:** To obtain the subject inhibitor containing an extract of leaf of Japanese chestnut, bur of Japanese chestnut and leaf of Eriobotrya japonica and keeping lubricity and softness of skin, suppressing activity of hyaluronidase decomposing hyaluronic acid for preventing aging and preventing fine wrinkles or dryness of skin.

**CONSTITUTION:** This inhibitor contains an extract of leaf of Japanese chestnut, bur of Japanese chestnut or leaf of Eriobotrya japonica with solvent. Furthermore, e.g. leaf of Japanese chestnut, bur of Japanese chestnut or leaf of Eriobotrya japonica is preferably extracted using water or a hydrophilic organic solvent such as ethanol. Concretely, 300ml purified water is added to 10g leaf of Japanese chestnut and the mixture is heated for 3hr and filtered and subjected to lyophilization, etc. For example, the inhibitor is added to a cosmetic raw material such as squalane and preferably used as a lotion, etc.

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**CLAIMS**

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[Claim(s)]

[Claim 1] Hyaluronidase inhibitor in which a leaf of a chestnut and \*\*\*\* contain a solvent extraction thing of a biwa leaf

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**DETAILED DESCRIPTION**

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**[Detailed Description of the Invention]****[0001]**

[Industrial Application] Many-years internal use of this invention is carried out as drugs of other purposes, etc., it maintains the lubricity of the skin, and pliability using the vegetable extract in which safety was guaranteed, controls the activity of the hyaluronidase which decomposes the hyaluronic acid which prevents aging, and relates to the hyaluronidase inhibitor which protects small JIWA of the skin, and with an umbrella.

**[0002]**

[Description of the Prior Art] the fallen-leaves tree to which a chestnut is distributed over Kyushu and the Korean Peninsula from southern Hokkaido Nishi -- Tsuyoshi -- being widely considered as edible in fact -- the leaf -- a chestnut leaf -- the \*\*\*\* is called a chestnut ball and applied externally by a Japanese lacquer rash, a heat rash, burn, etc. A biwa is called native [ of the China Nakaminami part ], and west of Kanto, widely, the leaf of \*\*\*\*\* is called biwa leaf and used for \*\*\*\*, an anti-diarrheal, urination, antitussive, etc. in Japan. The cell activation operation and the damage cure action are known by JP,62-67028,A.

**[0003]**

[Problem(s) to be Solved by the Invention] Apply to the skin, and it is safe, and the purpose of this invention is to provide a raw material with strong hyaluronidase inhibitory action.

**[0004]**

[Means for Solving the Problem] In order that this invention persons might solve the aforementioned technical problem, edible was already presented with them over many years, they screened and investigated vegetation with which safety to a human body is confirmed, and examined what has utility value as hyaluronidase inhibitor. As a result, a leaf of a chestnut and \*\*\*\* found out that it was a raw material whose biwa leaf of hyaluronidase inhibitory action is dramatically strong.

[0005]That is, this invention is hyaluronidase inhibitor in which a leaf of a chestnut and \*\*\*\* contain a solvent extraction thing of a biwa leaf.

[0006]A leaf of a chestnut and \*\*\*\* extract as a utilizing method of a biwa leaf with water or a hydrophilic organic solvent, for example, ethanol, methanol, acetone, etc. However, since it is extraction of a cosmetic material, naturally extraction with water, ethanol, or a mixed solvent of this is preferred. Depending on the case, mixture of polyhydric alcohol, such as glycerin, 1, three butylene glycols, and propylene glycol, or polyhydric alcohol, and water can also be used for extraction. It is also effective to freeze-dry and to use as a granular material depending on a utilizing method.

[0007]This substance can be added for moisturizers, various drugs, etc., such as solid oils, such as liquefied oils, such as other cosmetic materials, for example, squalane, and jojoba oil, yellow bees wax, and cetyl alcohol, various kinds of active agents, glycerin, 1, and 3 butylene glycol, and cosmetics of various dosage forms can be adjusted. For example, what is necessary is just to consider a usage pattern according to the purpose in a lotion, cream, a milky lotion, a pack, etc.

[0008]Hyaluronidase is widely distributed in a living body, is an enzyme which exists also in the skin and decomposes hyaluronic acid as the name suggests. Hyaluronic acid is a polymers polysaccharide of straight chain shape which beta-D-N-acetylglucosamine and beta-D-glucuronic acid combined by turns, and is a kind of GURIKOSAMINO glucan which exists in connective tissue of mammalian widely with chondroitin sulfate etc. As a function of hyaluronic acid within connective tissue, water is held to an intercellular space, and a cell is held, or the lubricity of the skin and pliability are maintained [ a jelly-like matrix is formed in an in-house, ], and it is thought that external force (mechanical obstacle) and bacterial infection are prevented. Hyaluronic acid of the skin decreases in number as it takes age, and it is said that aging smallness JIWA, with an umbrella, etc. is brought about as a result.

[0009]Therefore, it is thought that controlling the activity of hyaluronidase which decomposes this contributes to the stability of hyaluronic acid currently used for pharmaceutical preparation and stability of hyaluronic acid which existed in hyaluronic acid and the skin of pharmaceutical preparation after applying to the skin. Hyaluronidase being known also as an inflammation enzyme, and carrying out activity control suppressing inflammation, and working restrainedly also by allergy is known.

[0010]

[Example]Although the example which is a actual utilizing method is indicated below, this invention is not limited at all by this example. The example of the leaf of the chestnut used by this invention and the extract of \*\*\*\* of a chestnut is shown below.

[0011]300 ml of purified water is added to 10 g of leaves of example 1 chestnut, and it heats for 3 hours. It freeze-dried after filtering this.

[0012]Example 2 \*\*\*\* adds 300 ml of purified water to 10 g, and heats for 3 hours. It freeze-dried after filtering this.

[0013]It was neglected for five days, example 3 \*\*\*\* having added 300 ml of ethanol to 10 g, and sometimes agitating. This was freeze-dried after [ after evaporating ] filtration.

[0014]Example 4 \*\*\*\* adds 300 ml of purified water to 10 g, and heats a (dry article) for 3 hours. It freeze-dried after filtering this.

[0015]It was neglected for five days, having added 300 ml of distilled liquor (alcoholic 35%) to 10 g of example 5 biwa leaves, and sometimes agitating. This was freeze-dried after [ after evaporating ] filtration.

[0016]

Example 6 Lotion Olive-oil 0.5 Example 1. 0.5 HORIOKISHI ethylene (20E.0) SORUHI tongue monostearate 2.0 HORIOKISHI ethylene (60E.0) hydrogenated castor oil 2.0 ethanol 10.0 1.0% hyaluronate sodium solution 5.0 purified-water 80.0[0017]

Example 7 cream A Squalane 20.0. Olive oil 2.0 mink oil 1.0 jojoba-oil . 5.0 Yellow-bees-wax 5.0 Cetostearyl-alcohol . 2.0 Glycerol monostearate 1.0. Sorbitan monostearate 2.0 Example 2. 1.0B Purified water 47.9 HORIOKISHI ethylene (20E.0) SORUHI tongue monostearate 2.0 HORIOKISHI ethylene (60E.0) hydrogenated castor oil 1.0 glycerin 5.0 1.0% hyaluronate sodium solution . 5.0 Methyl parahydroxybenzoate 0.1A and B were measured, respectively, and it warmed to 70 \*\*, and after adding gradually, agitating A to B, it cooled to 30 \*\*, agitating slowly.

[0018]What example-8 changed the extract of Example 1 of example-6 into the extract of

Example 3, and was created [0019]What example-9 changed the extract of Example 2 of

example-7 into the extract of Example 4, and was created [0020]What example-10 changed

the extract of Example 1 of example-6 into the extract of Example 5, and was created [0021]

(Hyaluronidase activity inhibition test)

(Test method) 6 g of 0.4% hyaluronate sodium 0.1M (pH 6.0) phosphoric acid buffer solution is borrowed, a 37 \*\* constant temperature bath -- the 0.1 wt/v% solution (purified water when it is hard to dissolve, after adding ethanol and dissolving -- in addition) of after the neglect during 5 minutes, and said example (freeze-drying article) after evaporating and removing ethanol, it prepared so that it might become 0.1 wt/v% -- adding and agitating 1.0 ml -- 0.01% hyaluronidase (the product made from a sigma company make cow testis.) 1 ml of type I-S0.1M (pH 6.0) phosphoric acid buffer solution was added, it agitated promptly, and 6 was put into the Ostwald viscometer put into a 37 \*\* constant temperature bath. Viscosity was measured for this 1 minute, 5 minutes, 10 minutes, 20 minutes, and 40 minutes afterward. As contrast, pure water was added instead of the above-mentioned sample solution, and it measured similarly. In this examination, the final concentration of a sample will be 0.0125%. Viscosity of 1 minute after is set to 100, and a result is shown in Tables 1-7 as an index.

[0022]

[Table 1]

検体	5分後	10分後	20分後	40分後
対照	73.6	55.3	36.9	23.0
実施例1	99.5	99.7	99.6	99.5
実施例2	99.6	99.7	99.6	99.7
実施例4	99.5	99.4	99.4	99.1

[0023]

[Table 2]

検体	5分後	10分後	20分後	40分後
対照	70.8	51.1	33.1	20.8
実施例3	98.6	98.2	97.4	96.8
実施例5	99.0	99.0	99.2	99.3

[0024] Every six use test women's face was divided into right and left, and one side was made into the example, and by making another side into a comparative example, I had you use it once or more, and the questionnaire survey was conducted 3 previous month every day. A comparative example changes Examples 1 and 2 to water from Examples 6 and 7, respectively. (Comparative examples 1 and 2)

12 persons were divided into two groups and it experimented using the following sample.

実験No	使った試料
1	実施例6、7 比較例1、2
2	実施例8、9 比較例1、2
3	実施例10、7 比較例1、2

[0025]A judging standard is as follows and the following tables summarized the result of the questionnaire.

-3 with -2 very more sufficient comparative example in which -1 comparative example in which zero comparative example without 1 difference with 2 a little more sufficient example in which 3 example in which the example is very better is quite better is a little better is quite better

[0026]

実験No	肌荒れ防止	小皺の防止	しっとり感
1	18	17	16
2	18	16	18
3	19	18	18

[0027]

[Effect]The effect as an extract of this invention is the activity depressant action of hyaluronidase. Hyaluronidase is widely distributed in a living body, is an enzyme which exists also in the skin and decomposes hyaluronic acid as the name suggests. Hyaluronic acid is a polymers polysaccharide of the straight chain shape which beta-D-N-acetylglucosamine and beta-D-glucuronic acid combined by turns, and is a kind of the GURIKOSAMINO glucan which exists in the connective tissue of a \*\*\*\* animal widely with chondroitin sulfate etc. As a function of the hyaluronic acid within connective tissue, water is held to an intercellular space, and a cell is held, or the lubricity of the skin and pliability are maintained [ a jelly-like matrix is formed in an in-house ], and it is thought that external force (mechanical obstacle) and bacterial infection are prevented. The hyaluronic acid of the skin decreases in number as it takes age, and it is said that aging smallness JIWA, with an umbrella, etc. is brought about as a result.

Therefore, it is thought that controlling the activity of the hyaluronidase which decomposes this contributes to the stability of the hyaluronic acid currently used for pharmaceutical preparation and the stability of the hyaluronic acid which existed in the hyaluronic acid and the skin of pharmaceutical preparation after applying to the skin. Hyaluronidase being known also as an inflammation enzyme, and carrying out activity control suppressing inflammation, and working restrainedly also by allergy is known.

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